PCT/EP2004/010696

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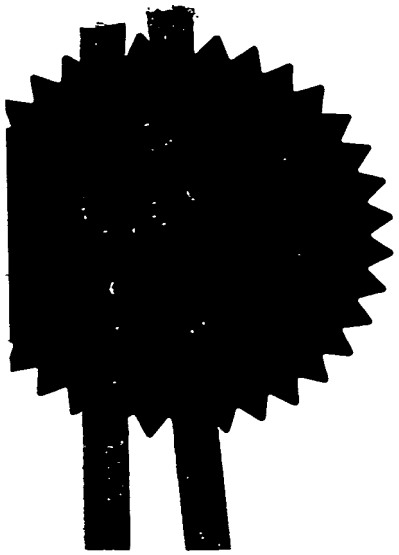

Signed A M Brewer

Dated 21 June 2004

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Request for grant of a patent

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1.	Your reference	3-33379P1
2.	Patent application number *(The Patent Office will fill in this part)*	0322371.6
3.	Full name, address and postcode of the or of each applicant *(underline all surnames)*	NOVARTIS CONSUMER HEALTH SA ROUTE DE L'ETRAZ CH-1260 NYON SWITZERLAND
	Patent ADP number *(if you know it)* If the applicant is a corporate body, give the country/state of its incorporation	SWITZERLAND 07220890001
4.	Title of invention	Coated Tablets
5.	Name of your agent *(If you have one)* "Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*	Craig McLean Novartis Pharmaceuticals UK Limited Patents and Trademarks Wimblehurst Road Horsham, West Sussex RH12 5AB
	Patents ADP number *(if you know it)*	07181522002
6.	If you are declaring priority from one ore more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number	Country / Priority application number *(if you know it)* / Date of filing (day/month/year)
7.	If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application	Number of earlier application / Date of filing (day/month/year)
8.	Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer 'Yes' if:* *a) any applicant named in part 3 is not an inventor, or* *b) there is an inventor who is not named as an applicant, or* *c) any named applicant is a corporate body.* *(see note (d))*	Yes

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Continuation sheets of this form	
Description	4
Claim(s)	1
Abstract	1
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10. If you are also filing any of the following, state how many against each item.

Priority documents	
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Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	
Request for preliminary examination and search *(Patents Form 9/77)*	
Request for substantive examination *(Patents Form 10/77)*	
Any other documents *(please specify)*	

11. I/We request the grant of a patent on the basis of this application

Signature — Date

Craig McLean — 24th September 2003

12. Name and daytime telephone number of person to contact in the United Kingdom

Mr. Trevor Drew — 01403 323069

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Coated Tablets

The present invention concerns coated tablets comprising the pharmaceutically active substance diclofenac, which tablets are characterized by a special, very beneficial coating.

Diclofenac is a widely used non-steroidal anti-inflammatory drug (NSAID), and in the context of this document the term "diclofenac" is to be understood as including diclofenac (free acid) and pharmaceutically acceptable salts thereof, e.g. diclofenac sodium, diclofenac potassium or diclofenac epolamine. In particular preferred is diclofenac K.

Diclofenac tablets with coatings are known in the art. The general purpose of a said coating is to protect the tablet core, including the active substance, against moisture, oxygen, chemical decomposition in general as well as mechanical abrasion and so to increase the stability, i.e. the shelf life, of the tablet. A polymer that is particularly well suited to form the basis of a film coating for diclofenac tablets is hydroxypropyl methylcellulose (HPMC). It is ideal in providing an effective moisture barrier and in general reduce permeability for gases. A corresponding film coated tablet comprising 12.5 mg diclofenac K is known in the art. Said film coated tablet is manufactured by first coating the tablet core with a white coating premix comprising HPMC, polyoxyethylene glycol 400, polyethylene sorbitan monooleate and titanium dioxide (as whitening dyestuff). The coated tablet core so obtained is then subjected to a second coating step with a clear coating premix comprising HPMC, polyoxyethylene glycol 400 and maltodextrin.

The downsides of said film coated diclofenac K tablet are as follows. As two coating steps have to be performed, the coating process is lengthy, rather complicated and in general difficult to perform. Moreover, an unsatisfactorily high amount of film coated tablets having defaults in their coatings, such as ridges or picking on their surface, are obtained. Thus, strict quality control is required and too many film coated tablets have to be sorted out. Furthermore, the taste of said twice coated tablet is not very pleasant due to the specific coating compositions used.

It is therefore a goal of the present invention to avoid said disadvantages and provide a diclofenac tablet with a film coating based on HPMC, which tablet can be manufactured by a

simpler process, within a shorter process time, with less defaults in coating, and which tablet is essentially tasteless.

Thus, the present invention concerns a film coated tablet comprising
(a) a tablet core comprising diclofenac or a pharmaceutically acceptable salt thereof, and
(b) a coating layer comprising HPMC, stearic acid and microcrystalline cellulose, which coating layer is completely enrobing the tablet core (a).

Preferably, the film coated tablet has one single coating layer (b).

More preferably, the film coated tablet consists essentially of (a) and (b) as defined hereinabove or hereinbelow. With respect to the tablet cores (a) this means, that, preferably, diclofenac is the only pharmaceutically active substance present.

Preferably, the coating layer (b) in addition comprises titanium dioxide as whitening dyestuff.

In the tablet core (a), diclofenac is typically present in an amount of 10-100 mg, preferably 10-50 mg. The coating of the present invention is particularly useful for enrobing tablet cores comprising diclofenac K. In particular, 12.5 mg of diclofenac K are used.

Preferably, the tablet core (a) comprises microcrystalline cellulose. By including microcrystalline cellulose into the composition of both the tablet core (a) and the coating layer (b), the compatibility between the core and the coating layer is enhanced. Typically, microcrystalline cellulose is present in an amount of 2-15%, preferably 5-10%, (w/w) of the tablet core composition.

In general, tablet cores (a) are composed of components well known in the art and are manufactured in a manner known per se.

Example 1: Film coated tablet comprising 12.5 mg Diclofenac K

Core composition

diclofenac K	12.5 mg
magnesium stearate	2.025 mg

povidone	4.05 mg
silica colloidal anhydrous	8.025 mg
cellulose, microcrystalline	13.5 mg
lactose monohydrate	33.45 mg
maize starch	99.75 mg

Coating composition

Mixture of HPMC, stearic acid, microcrystalline cellulose and titanium dioxide (e.g. "Sepifilm LP 770 White", company Seppic) 6.0 mg

Tablet cores are manufactured in a manner known per se, e.g. by direct compression of the finely powdered components of the core composition. The tablet cores are coated with the coating composition in a manner known per se, namely by following the instructions of the manufacturer, Seppic, for applying said coating composition.

Comparative Example 1: Film coated tablet comprising 12.5 mg Diclofenac K

Core composition

diclofenac K	12.5 mg
magnesium stearate	2.025 mg
povidone	4.05 mg
silica colloidal anhydrous	8.025 mg
cellulose, microcrystalline	13.5 mg
sodium starch glycolate	26.7 mg
lactose monohydrate	33.45 mg
maize starch	99.75 mg

Coating composition 1

Mixture of HPMC, Polyoxyethylene glycol 400 (= Macrogol 400), Polyethylene sorbitan monooleate (= Polysorbate 80) and titanium dioxide (e.g. Opadry® "White coating premix 13675", company Colorcon) 8.0 mg

Coating composition 2

Mixture of HPMC, Macrogol 400 and maltodextrin

(e.g. Opadry® "Clear coating premix 14003", company Colorcon) 1.0 mg

Tablet cores are manufactured in a manner known per se, e.g. by direct compression of the finely powdered components of the core composition. The tablet cores are coated in a two-step coating process first by coating it with coating composition 1 and then by coating it with coating composition 2 in a manner known per se, namely by following the instructions of the manufacturer, Colorcon, for applying said two coating compositions.

Comparison between Example 1 and Comparative Example 1:

	Example 1	Comparative Example 1
Number of coatings	1	2
Mass of coating (mg/tablet)	6	9
Process time	60 min	95 min
Process issues	none	ridges, picking on tablet surface
Taste of final product	tasteless	not pleasant

The great advantages of Example 1, both with respect to a simpler and shorter process and with respect to the properties of the final product, are evident.

Claims

1. A film coated tablet comprising
(a) a tablet core comprising diclofenac or pharmaceutically acceptable salt thereof, and
(b) a coating layer comprising hydroxypropyl methylcellulose, stearic acid and microcrystalline cellulose, which coating layer is completely enrobing the tablet core (a).

2. A film coated tablet according to claim 1, wherein the tablet core (a) comprises diclofenac potassium.

3. A film coated tablet according to claim 2, wherein diclofenac potassium is present in an amount of 10-50 mg.

4. A film coated tablet according to claim 2, wherein diclofenac potassium is present in an amount of 12.5 mg.

5. A film coated tablet according to any one of claims 1-4, wherein the tablet core (a) comprises microcrystalline cellulose.

6. A film coated tablet according to claim 5, wherein microcrystalline cellulose is present in the tablet core (a) in an amount of 2-15% (w/w).

7. A film coated tablet according to any one of claims 1-6, wherein the coating layer (b) in addition comprises titanium dioxide.

Coated Tablets

Abstract of the Disclosure

The invention relates to coated tablets comprising the pharmaceutically active substance diclofenac. Said tablets are characterized by a special, very beneficial coating based on hydroxypropyl methylcellulose.

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